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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,289	06/26/2003	Bernhard Lindenthal	SCH-1985	3274

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EXAMINER	
HUI, SAN MING R	
ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/606,289	LINDENTHAL ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-9-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed February 22, 2007 have been entered.

The addition of claims 12-16 is acknowledged.

Claims 1-16 are pending.

The outstanding rejections under 35 USC 101, 112, and 103(a) are withdrawn in view of the amendments and remarks filed February 22, 2007.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antagonizing the EP2 receptors by EP2 antagonist, does not reasonably provide enablement for other antagonizing method. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. In the instant case, the specification fails to to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a

disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to provide information allowing the skilled artisan to ascertain these compounds possessing the recited, and claimed, physiological activity without undue experimentation.

1) the quantity of experimentation necessary,

. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on all methods of antagonizing EP2 receptors including, but not limited to, antibodies and gene therapy necessitating an exhaustive search for all embodiments, regardless their chemical formula, immunological properties, or structure, suitable to practice the claimed invention. Examiner notes the claims read on all compounds or modalities possessing the envisioned physiological activity, disclosed, or undisclosed, regardless the

modalities desired. Additionally, those antibodies or gene vectors seen as encompassing such physiological activity must be experimentally discovered by the skilled artisan.

2) the amount of direction or guidance provided,

In the instant case, only a limited number of EP2 antagonists examples are set forth, thereby failing to provide sufficient working examples. Those compounds disclosed in the instant specification encompass only a small number of those compound classes envisioned as possessing physiological activity required to practice the invention as herein claimed. Absent that small genus of compounds herein recited, the instant specification is silent as to making, or using, those other compound genera or macromolecules such as proteins, peptides and genes encompassed by the instant claims. Although the specification directs the skilled artisan to specific compounds such as EP2 antagonists, the application is silent with regard to selection of any additional compounds structurally unrelated to those few compounds listed in the instant specification.

3) the presence, or absence, of working examples,

Applicant fails to set forth the criteria that structurally defines, or identifies, those compounds possessing EP2 antagonistic activity. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "EP2 antagonist" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define those structural classes of

compounds required to practice the invention as herein claimed, as required by those guidelines set forth in *In re Wands*, supra. Absent exemplification providing guidance as to these compound classes herein envisioned, the instant specification fails to place those compound classes possessing various structural formulas requiring specific physiological EP2 antagonistic activity in the skilled artisan's possession, absent undue experimentation.

4) the nature of the invention,

The instant invention reading on all possible compounds or modalities possessing theEP2 antagonistic activityenvisioned, disclosed, or undisclosed, set forth a broad inventive scope.

5) the state of the prior art,

The instant claims read on all modalities that would antagonize EP2 receptors, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Although various individual compounds possessing the disclosed EP2 receptors activity are known to those of skill in the art, no information is provided to guide the skilled artisan to those diverse genera of structurally divergent compounds possessing similar physiological activity. Examiner is unaware of any nexus, stated in the art, or herein disclosed, attributing the herein envisioned physiological activity to one, or another, structural formula. Simply stated the skilled artisan must employ experimentation to discover compounds possessing these EP2 antagonistic activities required to practice the claimed invention.

6) the relative skill of those in the art

Those individuals skilled in the art possess the required knowledge to perform those assays employed to identify compounds useful for practicing the invention as herein claimed. Applicants' failure to provide adequate guidance as to the envisioned structural formulas employed in the instant claims requires the skilled artisan to establish, by individual assay, each compound deemed suitable for use in the instant invention.

7) the breadth of the claims.

The instant claims read on all modalities that would antagonize EP2, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Examiner notes the instant claims fail to provide any guidance as to those structural embodiments inherent in those compounds possessing the EP2 antagonistic activity herein envisioned. Applicant's claims encompass every, and all, compounds providing the recited EP2 antagonistic activity regardless the structural formula of such compounds. Absent guidance with regard to the structural identifies of those compounds possessing the recited EP2 antagonistic activity, each compounds must be identified by experimentation in every case. Applicants fail to provide information sufficient to identify the structural formulas of those compounds useful to practice the claimed invention, absent undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Crofford et al. (Arthritis & Rheumatism, 2000;43(8):1891-1896).

Crofford et al. teaches 4 women taking COX-2 inhibitors. The effect of impairing cumulus expansion and oocyte maturation would be considered as inherently present in the women who took the COX-2 inhibitors.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breyer et al. (Annals of the New York Academy of Sciences (2000), 905 (Lysophospholipids and Eicosanoids in Biology and Pathophysiology), 221-231), Narumiya et al. Physiological Review, 1999;79(4):1193-1226, reference of record and Hizaki et al., (Proc. Natl. Acad. Sci. USA, 1999;96:10501-10506) in view of applicant's own admission on page 9, lines 10-21, Norel et al. (British Journal of Pharmacology, 1999;126:867-872) and Noble et al. (American Family Physician, 2000 Jun 15;61(12):3669-76).

Breyer et al. teaches the disruption of EP2 receptors and inhibition of COX-2 can inhibit the ovulation (Examiner notes: oocyte maturation), fertilization and implantation (See page 228 – 229).

Hizaki et al. also teaches the lacking of EP2 receptor in mice may lead to abortivce expansion of the cumulus and impaired ovulation (See particularly the abstract and page 10502 – 10505 Results Section).

Nirumiya et al. teaches a general review of EP receptors. Specifically, Nirumiya et al. teaches that the relationship between PGE2 and EP2 receptors in a way that PGE2 interacts with EP2 causing increase in cAMP which in result would induce oophorus maturation (See page 1217, Reproduction section).

The primary references do not expressly teach the use of AH6809 and COX-2 inhibitor such as celecoxib to control fertility or impair cumulus expansion and oocyte maturation.

Applicant's admission on the various prior arts teaching the administration of COX inhibitors such as rofecoxib would disrupt or inhibit the ovulation process and induce delayed follicular rupture.

Norel teaches AH6809 as a EP1/EP2 antagonists (See the abstract).

Noble et al. teaches celecoxib as a COX-2 inhibitor (See the abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to employ AH6809 and/or Celecoxib in a method of controlling fertility or impairing cumulus expansion and oocyte maturation.

One of ordinary skill in the art would have been motivated to employ AH6809 and/or Celecoxib in a method of controlling fertility or impairing cumulus expansion and oocyte maturation. It is known that the inhibition of EP2 activation and COX-2 would lead to impair ovulation, fertilization, implantation, and abortive expansion of cumulus. It is also known that the activation of EP2 receptor would induce oophorus maturation for fertilization. Therefore, employing any known EP2 antagonist, such as AH6809, and/or any known COX-2 inhibitors, such as celecoxib, to block the activation of EP2 and/or COX-2 would reasonably expect to lead to the impairment of ovulation, oocyte maturation, implantation, fertilization and abortive expansion of cumulus.

Response to Arguments

Applicant's arguments filed February 22, 2007 averring the cited prior arts' failure to teach a pharmacological agent to effect the herein claimed fertility control have been fully considered but they are not persuasive. Examiner notes that applicant is clearly aware of the use of COX inhibitors can disrupt or inhibit ovulation and induce follicular rupture. Given the closely association between oophorus maturation and EP2 receptors as discussed above, one of ordinary skill in the art would be motivated to employ a EP2 antagonist to inhibit or impair the maturation of oophorus, ovulation, oocyte maturation, implantation, fertilization and abortive expansion of cumulus even though the cited prior arts are lacking the teachings of using a EP2 antagonist to produce the recited effect. It is clear in the cited prior arts teachings that: 1) activation of EP2 promotes oophorus maturation; 2) the absebce or disruption of the EP2 receptors results in inhibit the

ovulation (Examiner notes: oocyte maturation), fertilization and implantation; and 3) the administration of COX inhibitors can lead to disruption or inhibition of the ovulation process and induction of delayed follicular rupture. Therefore, possessing the teachings of the cited prior arts, there is a strong suggestion and motivation to employ the herein claimed agents in the method of fertility control, absent evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1617